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(71) Applicant *(for all designated States except US)*: **MCLEAN HOSPITAL** [US/US]; 115 Mill Street, Belmont, MA 02478 (US).

(72) Inventors; and

(75) Inventors/Applicants *(for US only)*: **ROHAN, Michael, L.** [US/US]; 46 Hubbard Avenue, Cambridge, MA 02140 (US). **PAROW, Aimee** [US/US]; Apt. 16, 26 Allston Street, Allston, MA 02134 (US). **RENSHAW, Perry, F.** [US/US]; 6 Newton Road #2, Arlington, MA 02474 (US).

(74) Agents: **GLITZENSTEIN, Kurt** et al.; Fish & Richardson P.C., 225 Franklin Street, Boston, MA 02110-2804 (US).

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(54) Title: MAGNETIC FIELD STIMULATION TECHNIQUES

(57) Abstract: The invention involves enhancing brain function by stimulating the brain using magnetic fields. Applications of the new methods include improving the condition of individuals with cognitive disorders, such as depression, and studying the effects of neural stimulation using induced electric fields. These techniques can avoid deleterious effects of psychotropic pharmaceutical treatments, and provide a relatively safe, comfortable, inexpensive means of direct cranial stimulation.

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MAGNETIC FIELD STIMULATION TECHNIQUES

TECHNICAL FIELD

This invention relates to magnetic stimulation techniques, and more particularly to neural stimulation using a magnetic field.

BACKGROUND

Repetitive transcranial magnetic stimulation (rTMS) has been used with the goal of treating depression, see, *e.g.*, George et al., *The Journal of Neuropsychiatry and Clinical Neurosciences*, 8:373, 1996; Kolbinger et al., *Human Psychopharmacology*, 10:305, 1995.

One example of an rTMS technique uses a figure-8 surface coil with loops that are 4 cm in diameter (Cadwell, Kennewick, WA). This coil is placed next to the scalp, and is usually positioned to direct the magnetic field at the prefrontal cortex of the brain, see, *e.g.*, George et al., *The Journal of Neuropsychiatry and Clinical Neurosciences*, 8:373, 1996. An electric current is run through the magnetic coil to generate a magnetic field, specifically a sequence of single-cycle sinusoidal pulses where each pulse has a frequency of approximately 1800 Hz (or about 560 microseconds per pulse). These pulses are delivered at a repetition rate of 1 to 20 Hz (i.e., one pulse every 0.05 to 1 second), see, *e.g.*, George et al, *Biological Psychiatry*, 48:962, 2000; Eschweiler et al, *Psychiatry Research: Neuroimaging Section*, 99:161, 2000.

Some subjects have declined participation in rTMS studies due to pain induced in the scalp. In addition, seizures have been reported as a result of rTMS treatment, see, George et al, *Biological Psychiatry*, 48:962, 2000; Wasserman, *Electroencephalography and Clinical Neurophysiology* 108:1, 1998.

SUMMARY

The invention concerns enhancing brain function using novel magnetic field techniques. These magnetic field techniques use low field strengths, high repetition rates, and uniform gradients to improve brain function.

In one aspect of the present invention, a subject is selected for enhancement of brain function using a magnetic field. The subject's head is then subjected to a time-varying magnetic field having a maximum strength of less than about 50 G.

Advantages of this aspect of the invention include the following. Subjects with cognitive impairments may benefit from the new treatment by the lessening of the severity of the condition. Treatment techniques using this method can be administered inexpensively with relative safety and comfort, and offer a substitute for or complement to treatment by medication. Applications of the new methods include improving the condition of individuals with cognitive disorders, such as depression, and studying the effects of brain stimulation using induced electric fields.

Embodiments of this aspect of the invention can include one or more of the following features. After treating the subject (*e.g.*, a human patient), the subject can be evaluated for enhanced brain function. The magnetic field can have a maximum strength of less than about 10 G. The field can also be a gradient magnetic field (*i.e.*, a field in which the magnitude of a vector component of the magnetic field, expressed as the vector sum of the partial derivatives with respect to the three coordinate variables *x*, *y*, and *z*, per unit distance, changes along one or more directions) that is substantially uniform (*e.g.*, to within 10%) and unidirectional over the relevant volume (*e.g.*, the entire brain, or a region of interest of the brain such as the prefrontal cortex). The gradient of the magnetic field can be less than about 5 G/cm. The magnetic field can be generated using a sequence of trapezoidal pulses of alternating polarity, where each pulse has a duration of about 1 millisecond.

In another aspect of the present invention, a subject is selected for enhancement of brain function using a magnetic field. The subject's head is then subjected to a time-varying gradient magnetic field that is substantially uniform and unidirectional.

In another aspect of the present invention, a subject is selected for enhancement of brain function using a magnetic field. The subject's head is then subjected to a time-varying magnetic field generating by a sequence of pulses, each having a duration of less than about 10 milliseconds.

Unless otherwise defined, all technical and scientific terms used herein have the same meaning as commonly understood by one of ordinary skill in the art to which this invention belongs. Although methods and materials similar or equivalent to those described herein can be used in the practice or testing of the present invention, suitable methods and materials are

described below. All publications, patent applications, patents, and other references mentioned herein are incorporated by reference in their entirety. In case of conflict, the present specification, including definitions, will control. In addition, the materials, methods, and examples are illustrative only and not intended to be limiting.

The details of one or more embodiments of the invention are set forth in the accompanying drawings and the description below. Other features, objects, and advantages of the invention will be apparent from the description and drawings, and from the claims.

DESCRIPTION OF DRAWINGS

FIG. 1 is a diagram of a system and apparatus for administering the present magnetic field treatments.

FIG. 2 is an example of a magnetic field waveform used in the present magnetic field treatment methods.

FIG. 3 is a three-dimensional plot of a magnetic field used in the present magnetic field treatment methods.

FIG. 4 is an example of an electric field waveform induced using the present magnetic field treatment methods.

FIG. 5 is a contour plot of an electric field used in the present magnetic field treatment methods.

FIG. 6 is a three-dimensional plot of an electric field used in the present magnetic field treatment methods.

FIG. 7 is a table of the effects of the present treatment on the mood of 32 depressed subjects over 102 visits and 15 comparison subjects over 23 visits.

FIG. 8 is a table of the effects of the present treatment at the first visit on the mood of medication-naïve and non-naïve bipolar subjects receiving treatment as well as bipolar subjects receiving sham treatment and comparison subjects receiving treatment.

FIG. 9 is a graph of mood change for all bipolar patients over the course of four treatments.

FIG. 10 is a graph of depression level for all bipolar patients over the course of four treatments.

FIG. 11 is a graph of mood change for all bipolar patients who underwent all four treatments.

FIG. 12 is a graph of depression level for all bipolar patients who underwent all four treatments.

FIG. 13 is a graph of mood change for all patients who had no change in medication over the course of three treatments.

FIG. 14 is a graph of depression level for all bipolar patients who had no change in medication over the course of three treatments.

FIG. 15 is an example of a magnetic field waveform used in an example of repetitive transcranial magnetic stimulation.

FIG. 16 is a three-dimensional plot of a magnetic field used in an example of repetitive transcranial magnetic stimulation.

FIG. 17 is an example of an electric field waveform induced using an example of repetitive transcranial magnetic stimulation.

FIG. 18 is a contour plot of an electric field used in an example of repetitive transcranial magnetic stimulation.

FIG. 19 is a three-dimensional plot of an electric field used in an example of repetitive transcranial magnetic stimulation.

DETAILED DESCRIPTION

Apparatuses and Systems

A device 10 according to the present invention is shown in FIG. 1. The device 10 has a magnetic coil 12, an amplifier 14, and a waveform generator 16. The waveform generator 16 (*e.g.*, a general-purpose programmable computer or a purpose-built electric circuit) provides an electrical pulse sequence to the amplifier 14, which amplifies the electrical signals and provides them to the magnetic coil 12.

The magnetic coil 12 produces a magnetic field in response to electrical signals received from the amplifier 14. Over the region in which the subject's brain is positioned, the magnetic field is a gradient magnetic field that is substantially uniform (i.e., the magnetic field strength varies substantially linearly in only one direction, *e.g.*, at about 5 G/cm, with the variation occurring from anterior to posterior across the subject's head) and unidirectional (i.e., the vectors representing the magnetic field all point in substantially the same direction, *e.g.*, along the long axis of the subject's body). (Alternatively, a magnetic coil can be used that generates a substantially uniform and unidirectional gradient magnetic field over only a

region of interest of the brain, *e.g.*, the left prefrontal cortex.) The magnetic coil 12 is large enough to accommodate a subject's head, with a diameter of, *e.g.*, about 35 cm (14 in.).

When being treated with device 10, the subject 18 lays down on a standard patient gurney 20 with a head support 22, with his or her head positioned inside the coil 12.

Other devices can also be used for administering the present treatment method. For instance, a conventional magnetic resonance imaging apparatus can be used. Alternatively, instead of using a device such as device 10 that consists of separate components, the device can instead integrate one or more components, *e.g.*, to make the device easily portable. Alternatively or additionally, the magnetic coil can be included in a hat-like structure, and the waveform generator, amplifier, and power source (*e.g.*, a battery) integrated into a control mechanism that the subject carries or wears, *i.e.*, on his or her subject's belt. The subject can self-administer the treatment, and the treatment can be applied while the subject is lying down, standing, sitting, or in motion. Alternatively or additionally, the control device can be pre-set to administer the treatment for specific periods at specific intervals or continuously.

Methods

Prior to receiving treatment using device 10, a subject is selected as a candidate for enhancement of brain function. This selection is generally performed by medical professionals, *e.g.*, because the subject has been diagnosed as suffering a cognitive impairment. Alternatively, a subject could self-select based on a perceived need or desire to enhance brain function. Selection can be based on either subjective or objective criteria, including, *e.g.*, anxiety, moodiness, depression, lethargy, sleepiness, learning difficulties, and memory impairments.

To administer the treatment, the subject's head is positioned inside coil 12, and subjected to a time-varying magnetic field. (Alternatively, the subject's entire body could be positioned inside a full-body coil, and subjected to a magnetic field.)

The magnetic pulse train used to generate the time-varying magnetic field is shown in FIG. 2. The pulse train comprises a sequence of pulses delivered at a high rate. As discussed in detail below, the magnetic field induces an electrical field in the subject's brain. This electrical field can interact with neurons to cause cognitive effect. In light of this, the duration of each individual magnetic pulse is selected to be on the order of the refractory period of an axon, *i.e.*, on the order of several milliseconds (*e.g.*, 1 to 10 milliseconds), see, *e.g.*, E. R Kandel et al., *Principles of Neural Science*, 1991, which is incorporated by

reference herein. Thus, the pulse duration can be from on the order of 0.5 milliseconds to 10 milliseconds.

For example, each pulse has a trapezoidal shape, with 128 microsecond ramp times (from zero to plateau) and 768 microsecond plateau times (for a total duration of 1.024 milliseconds). The pulses alternate in polarity, with a short gap between successive pulses. A single pulse train comprises 512 successive pulses, and so lasts for about a half-second. After a delay of about a second-and-a-half, the pulse train is repeated (giving one pulse train every two seconds), and the treatment concludes after about six hundred repetitions (for a total treatment time of about 20 minutes). Alternatively, the second-and-a-half delay between successive pulse trains can be eliminated.

At the plateau of each trapezoidal pulse, the maximum magnetic field strength is on the order of 5-10 G, with a magnetic field gradient of 0.33 G/cm. FIG. 3 shows a three-dimensional plot of the resultant magnetic field. Pulse sequences yielding maximum magnetic field strengths of up to about 50 G, and maximum magnetic field gradients of up to about 5 G/cm, can alternatively be used.

These magnetic fields induce electric fields in the subject's brain. The characteristics of these electric fields are defined by the magnetic field parameters according to Maxwell's equation: $\nabla \times E(x,y,z,t) = -\partial B(x,y,z,t)/\partial t$, where $\nabla \times E$ is the curl of the electric field and $\frac{\partial B}{\partial t}$ is the rate of change of the magnetic field over time. In Cartesian coordinates, this equation becomes:

$$\partial E_x/\partial y - \partial E_y/\partial x = -\partial B_z/\partial t,$$
$$\partial E_y/\partial z - \partial E_z/\partial y = -\partial B_x/\partial t,$$
$$\partial E_z/\partial x - \partial E_x/\partial z = -\partial B_y/\partial t,$$

where the subscripts x, y, and z denote the component of the fields along those respective axes, see, *e.g.*, J.D. Jackson, *Classical Electrodynamics*, 1975, which is incorporated herein by reference.

These equations describe fields in free space (i.e., fields produced in the absence of other material). When conductive matter, such as brain tissue, is placed in the changing magnetic field, a charge distribution is also induced, resulting in an electric field. This electric field will affect the overall electric field in the head. This charge distribution can alter the free space electric field by up to about 50%, see Roth et al., *Electroencephalography*

and Clinical Neurophysiology, 81:47, 1991, which is incorporated herein by reference. The pattern of the effect of the charge distribution will depend on the shape and placement of the subject's head.

Two local field distributions are of particular interest. In the first, the *z*-component (superior-inferior component) of the magnetic field has a uniform gradient in the *y*-direction (anterior-posterior direction), and the *y*-component has a uniform gradient in the *z*-direction: $(B_x = 0, B_y = G(t)z,\ B_z = G(t)y)$, where G(t) is the value of the gradient. In this case, the electric field is given by: $(E_x = E_0(t) + \frac{1}{2}(\partial G(t)/\partial t)\cdot(y^2 - z^2),\ E_y = 0, E_z = 0)$, where $E_0(t)$ is a spatially constant field term that depends on the size of the coil and, consequently, the extent of the magnetic field. The preceding field description applies equally for the two other orientations, which is obtained by replacement of *x* with *y*, *y* with *z*, and *z* with *x* or by replacement of *x* with *z*, *y* with *x* and *z* with *y*, in both the vector components and coordinates. In addition, a given vector combination of these three field components, which forms an equivalent but rotated field, is also appropriate. Thus, one approach to applying the new treatment techniques involves using a magnetic field that has a vector component with a gradient that is substantially uniform, *e.g.*, to within 10%, in value or direction over a relevant volume of the subject's brain, *e.g.*, a 8 cm^3 volume or the left prefrontal cortex.

In another magnetic field distribution, the magnetic field is uniform over a local volume, which can be expressed as: $(B_x = 0, B_y = 0, B_z = B(t))$. The corresponding local electric field is: $(E_x = E_0(t) - a(\partial B(t)/\partial t)\cdot y, E_y = E_0(t) - (1-a)(\partial B(t)/\partial t)\cdot y,\ E_z = 0)$, where *a* is an arbitrary parameter determined by the details of coil winding.

In both situations, if $E_0(t)$ is sufficiently large compared to $\partial G(t)/\partial t \cdot R^2$ or $\partial B(t)/\partial t \cdot R$, where *R* is an effective radius of the volume of interest, *e.g.*, the radius of a subject's brain, then the local electric field is substantially uniform. The preceding field description applies equally for other orientations and rotations.

FIG. 4 shows the electric field waveform induced in the subject's brain when subjected to the magnetic field waveform shown in FIG. 2. The electric field waveform is a sequence of alternating monophasic square pulses of alternating polarity. The width of each induced electric pulse corresponds to the ramping period for the magnetic field pulses, *i.e.*, 256 microseconds. For the 0.33 G/cm magnetic field pulse amplitude, the electric field amplitude is approximately 0.7 V/m. This electric field strength is approximately an order of

magnitude less than the minimum peripheral nerve stimulation threshold of approximately 6-25 V/m, see, *e.g.*, J. P. Reilly, *Medical and Biological Engineering and Computing*, 27:101, 1989, thus providing an appropriate margin of safety against causing pain or seizures in the patient.

FIGS. 5 and 6 are contour and three-dimension plots of this electric field, respectively. These plots were made by modeling with Biot-Savart style integration, see, *e.g.*, J.D. Jackson, *Classical Electrodynamics*, 1975, which is incorporated herein by reference, for free space values using a magnetic field with a vector component having a gradient that is substantially uniform in value and direction. The plots in FIGS. 5 and 6 show that the electric field is substantially uniform in direction and changes slowly with distance. The direction of the induced electric field is determined by Maxwell's equations. For a magnetic field that has a gradient oriented from anterior to posterior across the subject's head, the induced electric field is oriented in from right to left across the subject's head.

EXAMPLES

Experiment

Forty-two people exhibiting symptoms of bipolar disorder and 15 comparison subjects were selected by medical professionals and subjected to the present method. The treatments were administered using a General Electric 1.5T Signa MRI scanner. After optional water suppression, slice selective excitation, and a spatial phase encoding pulse, the device applied a train of 512 trapezoidal alternating-polarity magnetic field pulses. These pulses were about one millisecond long, with ramp times of 128 microseconds and 768 microsecond plateau times. During the plateau of each pulse, the gradient was 0.33 G/cm, and the maximum magnetic field in the cortex was about 5 G. The entire train of 512 pulses was repeated every 2 seconds, six hundred times, for a total treatment time of 20 minutes. FIG. 3 is a three-dimensional plot of this magnetic field, and FIG. 2 is a diagram of the pulse train. The 'Y' gradient coil in the magnetic resonance scanner, having an approximate diameter of about 90 cm (36 in.), was used to apply this sequence, orienting the gradient in the anterior-posterior direction for the supine subjects. The gradient of the z-component of the magnetic field from this coil in the y-direction is uniform in both magnitude and direction over a subject's brain to within about 5%.

The magnetic field induced an electric field in the brains of the subjects. This electric field was oriented from right to left, from the subject's perspective, and had a magnitude of approximately 0.7 V/m. FIGS. 5 and 6 respectively show contour and three-dimension plots of this electric field modeled for free space values using a wire pattern for a coil similar to the 'Y' gradient coil in the Signa MRI system and computed with Biot-Savart style integration. The induced electric field consisted of 256 microsecond monophasic square pulses, where each pulse has a single polarity and an amplitude of approximately 0.72 V/m. A diagram of this electric field waveform is shown in FIG. 4. To achieve the same electric field with a smaller coil, Maxwell's equations show that a higher magnetic field is needed. Using a coil with a similar shape but smaller diameter, e.g., a "head-sized" 35 cm (14 in.) coil instead of a 36-inch "whole-body" gradient coil, to induce a similar same electric field magnitude would employ a magnetic field that reaches approximately 50 G in the head. The magnetic field used to induce such an electric field can have a vector component with a gradient that is slightly less uniform in value and direction, varying by about 10% over the cranial volume. In addition, a higher magnetic field, *e.g.*, 100 G, can be used with a smaller coil that provides a vector component with a substantially uniform gradient over only a region, e.g., 8 cm^3, of the brain.

Thirty-two subjects exhibiting symptoms of bipolar disorder reported a post-treatment overall mood improvement of at least one point on the Brief Affect Scale (BAS), which involves asking a subject to rate his mood after treatment compared to his mood at an earlier time, using a seven point scale: (1) very much improved, (2) much improved, (3) minimally improved, (4) no change, (5) minimally worse, (6) much worse, or (7) very much worse. Out of a total of 102 treatments of these 32 persons, 54 resulted in mood improvement, 40 resulted in no change, and 8 resulted in mood worsening according to the BAS. Comparison subjects also reported mood improvement in 5 of 23 total treatments. These results are given in the table in FIG. 7. In a sham trial where 10 subjects with bipolar disorder underwent sham treatments, mood improvement was reported in 3 of 10 visits, while 2 visits resulted in reports of mood worsening.

The study population was split into 3 groups: the first group (n=32) included subjects with bipolar disorder that had treatments. The second group (n=10) included subjects with bipolar disorder that underwent a sham treatment. The third group (n=15) included healthy comparison subjects that underwent the treatment. The first group, subjects with bipolar

disorder and undergoing treatments, was further split for comparisons involving the first visit only (n=30 first visits) for subjects that were not undergoing medication with a mood stabilizer such as lithium or depakote before the exam (naïve, n=11) and those that were taking mood stabilizers (n=19).

The table in FIG. 8 shows the BAS changes for these groups for the first visit. Twenty-three of 30 bipolar subjects reported improvement on their first visits. All 11 medication-naïve subjects reported mood improvement, and 3 of 10 bipolar subjects (and 4 of 14 comparison subjects) also reported improvement. The mean BAS improvement score for the first visit was higher for the subjects with bipolar disorder (0.87±0.68) than subjects with bipolar disorder who received the sham treatment (0.30±1.06) or comparison subjects (0.29±0.47). The medication naïve subset of the subjects with bipolar disorder had the highest mean BAS improvement score (1.18±0.41), which was greater than the subjects with bipolar disorder that were not medication naïve (0.68±0.75).

FIG. 9 shows the BAS and FIG. 10 shows the Hamilton Depression Scale (HAMD), see M. Hamilton, J. Neurosurg. Psychiatry 23:56, 1960, which is incorporated herein by reference, scores plotted against treatment number for treatments 1 through 4 for subjects with bipolar disorder; only a few subjects had more than 4 treatments. The BAS scores show self-rating of mood improvement for each treatment, and the HAMD depression ratings show a trend of reduced depression during the course of the 4 treatments, which occurred over approximately one month. The number of subjects decreased from 41 at the first treatment to 11 at the fourth treatment. FIG. 11 shows the BAS and FIG. 12 shows the HAMD scores for the 10 bipolar subjects that underwent all four treatments. FIGS. 11 and 12 also show mood improvement according to the BAS and reduction in depression according to the HAMD. FIG. 13 shows the BAS and FIG. 14 shows the HAMD scores for the 8 subjects that had no change in medication (*i.e.*, maintained the same mood-stabilization medication) over the course of 3 treatments. The BAS mood change scores showed a decreasing trend and the reduction in depression according to the HAMD was smaller for these subjects.

Comparative Example

One example of an rTMS technique uses a figure-8 surface coil with loops that are 4 cm in diameter (Cadwell, Kennewick, WA). This coil is placed next to the scalp, and is usually positioned to direct the magnetic field at the prefrontal cortex of the brain, see, *e.g.*,

George et al., *The Journal of Neuropsychiatry and Clinical Neurosciences*, 8:373, 1996. An electric current is run through the magnetic coil to generate a magnetic field, specifically a sequence of single-cycle sinusoidal pulses where each pulse has a frequency of approximately 1800 Hz (or about 560 microseconds per pulse). These pulses are delivered at a repetition rate of 1 Hz (i.e., one single-cycle sinusoidal pulse every 1 second), see, *e.g.*, George et al, *Biological Psychiatry*, 48:962, 2000; Eschweiler et al, *Psychiatry Research: Neuroimaging Section*, 99:161, 2000. This waveform is shown in FIG. 15. As the repetition period is much longer than the time span on the *x*-axis, only one single-cycle sinusoidal pulse appears in FIG. 15.

The magnetic field generated by the FIG. 15 waveform is shown in FIG. 16. The field reaches its maximum strength of approximately 10,000 G at the face of the coil. The strength of this magnetic field decreases rapidly as the distance from the coil increases, to about 0 G at about 6 cm to 8 cm, see, *e.g.*, Cohen et al, *Electroencephalography and Clinical Neurophysiology*, 75:350, 1990.

FIG. 17 shows the electric field waveform induced in the subject's brain by the magnetic field shown in FIG. 16. This waveform consists of a series of 560-microsecond single-cycle cosine pulses that repeat every 1 Hz.

FIG. 18 shows the contour plot and FIG. 19 shows the three-dimensional plot of the electric field induced in free space by the magnetic field shown in FIG. 16. The electric field is approximately 120 V/m at the face of the coil, and falls to about 0.02 V/m on the side of the head opposite the coil. The contours of this rapidly diminishing electric field reflect the shape of the figure-8 surface coil with 4 cm diameter loops, tilted at 45°, and placed 6.7 cm vertically and horizontally from a position equivalent to the center of the head: the electric field forms roughly circular loops.

A number of embodiments of the invention have been described. Nevertheless, it will be understood that various modifications may be made without departing from the spirit and scope of the invention. Accordingly, other embodiments are within the scope of the following claims.

WHAT IS CLAIMED IS:

1. A method of enhancing brain function, comprising:
   (a) selecting a subject for enhancement of brain function using a magnetic field;
   (b) generating a time-varying magnetic field with a maximum strength of less than about 50 G using a sequence of pulses, wherein the duration of each pulse in the sequence is about 1 millisecond; and
   (c) subjecting the subject's head to the time-varying magnetic field.
2. A method of enhancing brain function, comprising:
   (a) selecting a subject for enhancement of brain function using a magnetic field;
   (b) generating a time-varying magnetic field with a maximum strength of less than about 50 G; and
   (c) subjecting the subject's head to the time-varying magnetic field.
3. The method of claim 2, further comprising:
   (d) evaluating the subject for enhanced brain function after subjecting the subject to the magnetic field.
4. The method of claim 2, wherein the maximum magnetic field strength is less than about 10 G.
5. The method of claim 2, wherein the magnetic field is a gradient magnetic field that is substantially uniform over at least a region of the brain.
6. The method of claim 5, wherein the gradient is less than 5 G/cm.
7. The method of claim 2, wherein the magnetic field is a gradient magnetic field that is substantially unidirectional over at least a region of the brain.
8. The method of claim 7, wherein the region is a prefrontal cortex.
9. The method of claim 2, wherein
   the subject's head has a first side and a second side opposite the first side;
   the magnetic field is a gradient magnetic field; and
   the gradient is substantially oriented from the first side to the second side.
10. The method of claim 9, wherein the first side is an anterior side of the head according to the subject and the second side is a posterior side of the head.
11. The method of claim 2, wherein the subject is human.

12. The method of claim 2, wherein a sequence of pulses is used to generate the magnetic field, and wherein each pulse in the sequence is trapezoidal.
13. The method of claim 12, wherein successive pulses in the sequence have alternating polarity.
14. A method of enhancing brain function, comprising:
    (a) selecting a subject for enhancement of brain function using a magnetic field;
    (b) generating a time-varying gradient magnetic field that is substantially uniform and unidirectional; and
    (c) subjecting the subject's head to the time-varying magnetic field.
15. The method of claim 14, wherein the magnetic field is generated using a coil having a diameter greater than about 35 cm.
16. The method of claim 14, further comprising:
    (d) evaluating the subject for enhanced brain function after subjecting the subject to the magnetic field.
17. The method of claim 14, wherein the maximum magnetic field strength is less than about 10 G.
18. The method of claim 14, wherein the gradient is less than about 5 G/cm.
19. The method of claim 14, wherein the head has a first side and a second side opposite the first side and the gradient is substantially oriented from the first side to the second side.
20. The method of claim 19, wherein the first side is an anterior side of the head according to the subject and the second side is a posterior side of the head.
21. The method of claim 14, wherein the subject is human.
22. The method of claim 14, wherein a sequence of pulses is used to generate the magnetic field, and wherein each pulse in the sequence is trapezoidal.
23. The method of claim 14, wherein successive pulses in the sequence have alternating polarity.
24. A method of enhancing brain function, comprising:
    (a) selecting a subject for enhancement of brain function using a magnetic field;
    (b) generating a time-varying magnetic field using a sequence of pulses, wherein the duration of each pulse in the sequence is less than about 10 milliseconds; and
    (c) subjecting the subject's head to the time-varying magnetic field.

25. The method of claim 24, wherein the duration of each pulse in the sequence is about 1 millisecond.
26. The method of claim 24, further comprising:
(d) evaluating the subject for enhanced brain function after subjecting the subject to the magnetic field.
27. The method of claim 24, wherein the magnetic field is a gradient magnetic field that is substantially uniform over at least a region of the brain.
28. The method of claim 27, wherein the gradient is less than about 5 G/cm.
29. The method of claim 24, wherein the magnetic field is a gradient magnetic field that is substantially unidirectional over at least a region of the brain.
30. The method of claim 29, wherein the region is a prefrontal cortex.
31. The method of claim 24, wherein
the head has a first side and a second side opposite the first side;
the magnetic field is a gradient magnetic field; and
the gradient is substantially oriented from the first side to the second side.
32. The method of claim 31, wherein the first side is an anterior side of the head according to the subject and the second side is a posterior side of the head.
33. The method of claim 24, wherein the subject is human.
34. The method of claim 24, wherein each pulse in the sequence is trapezoidal.
35. The method of claim 34, wherein successive pulses in the sequence have alternating polarity.

FIG. 1

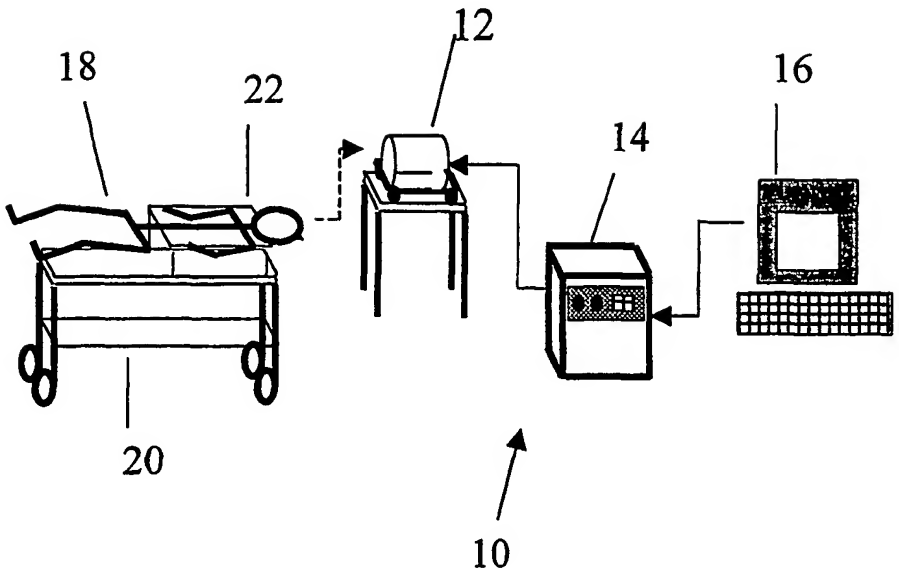


FIG. 2

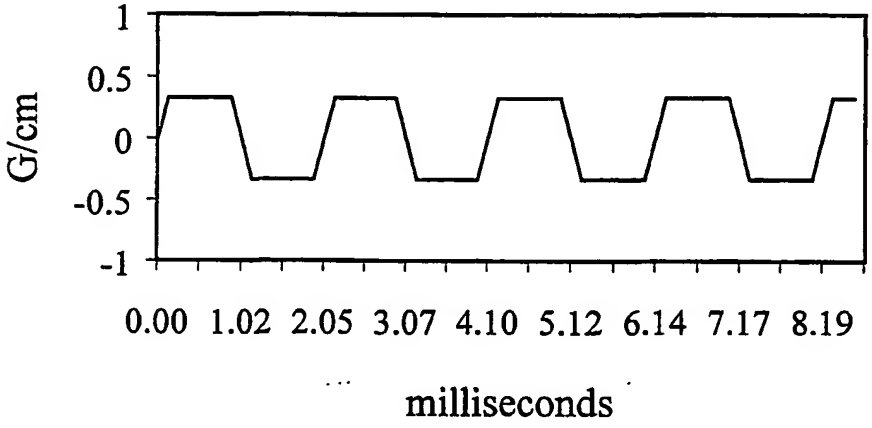

1
0.5
0
-0.5
-1
G/cm
0.00 1.02 2.05 3.07 4.10 5.12 6.14 7.17 8.19
milliseconds

FIG. 3

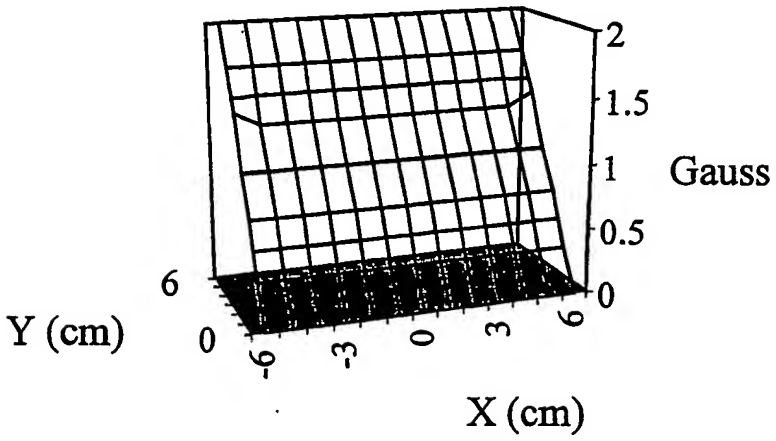

2
1.5
1
0.5
0
Gauss
6
0
Y (cm)
-6
-3
0
3
6
X (cm)

FIG. 4

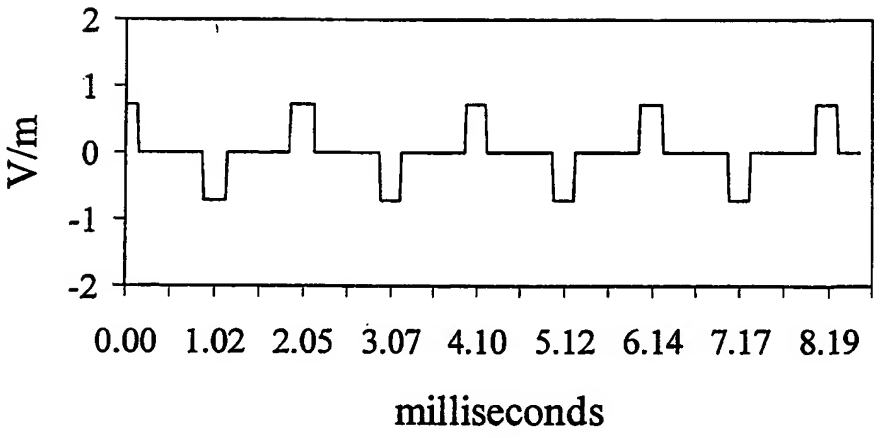


FIG. 5

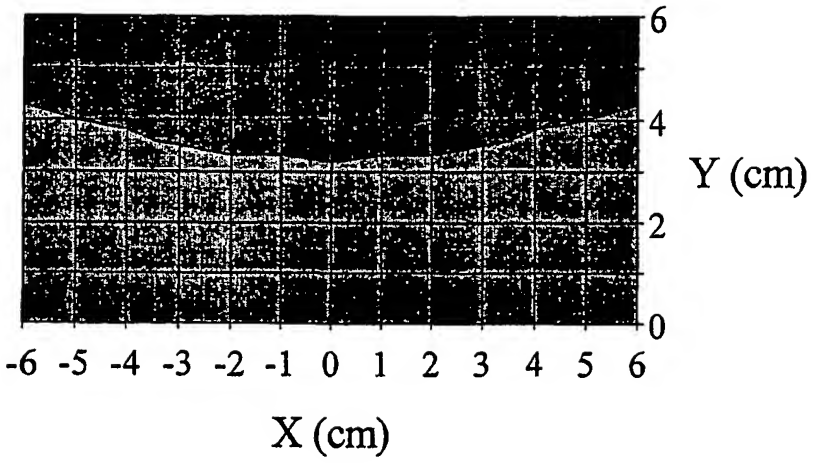
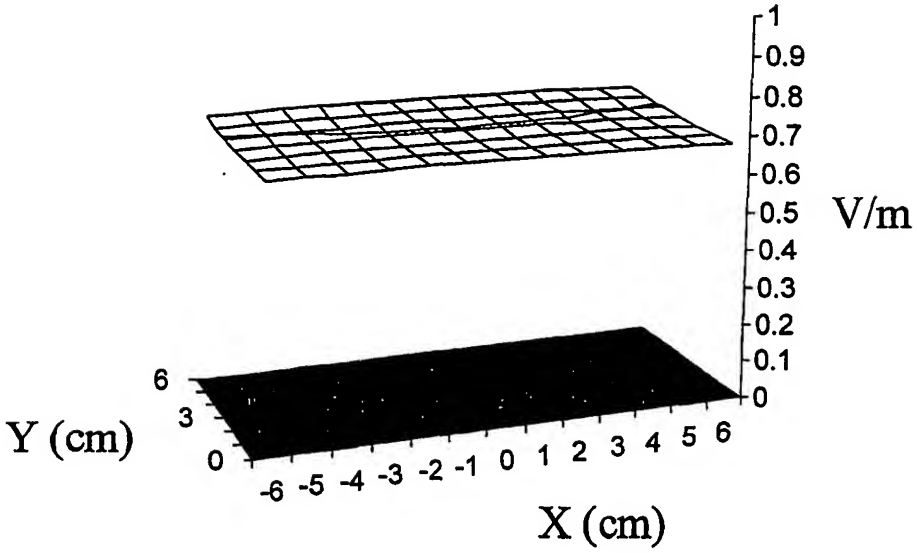

6
4
2
0
Y (cm)
-6 -5 -4 -3 -2 -1 0 1 2 3 4 5 6
X (cm)

FIG. 6


1
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
V/m
6
3
0
Y (cm)
-6 -5 -4 -3 -2 -1 0 1 2 3 4 5 6
X (cm)

	# total	# improved	Total visits	# worsened	Mean BAS	% improved
Bipolar subjects, MRSI	32	54	102	8	3.39±.85	53%
Comparison subjects, MRSI	15	5	23	0	3.78±.42	22%

FIG. 7

	# total	# improved	# worsened	% improved	Mean BAS
Bipolar subjects, MRSI	30	23	1	77%	3.13±0.68
subgroup: medication naïve	11	11	0	100%	2.82±0.41
subgroup: not naïve	19	12	1	63%	3.32±0.75
Bipolar subjects, sham MRI	10	3	2	30%	3.70±1.06
Comparison subjects, MRSI	15	4	0	27%	3.71±0.47

FIG. 8

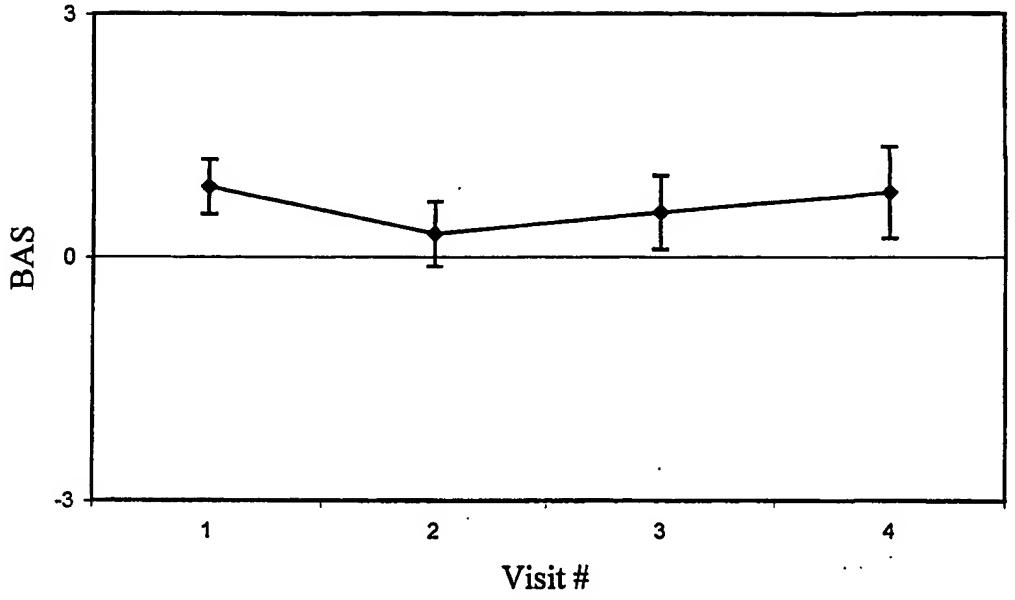


FIG. 9

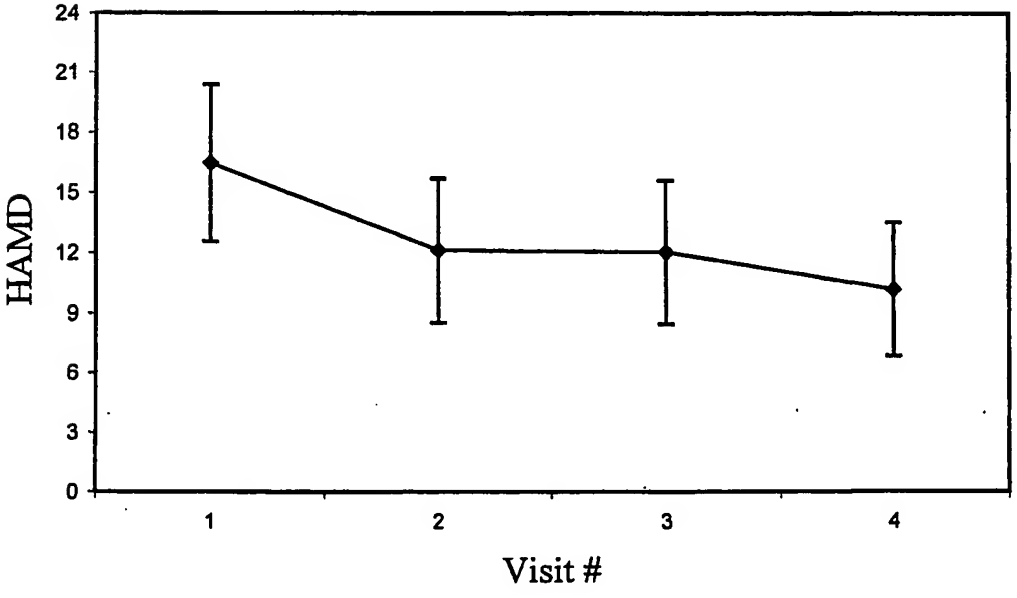


FIG. 10

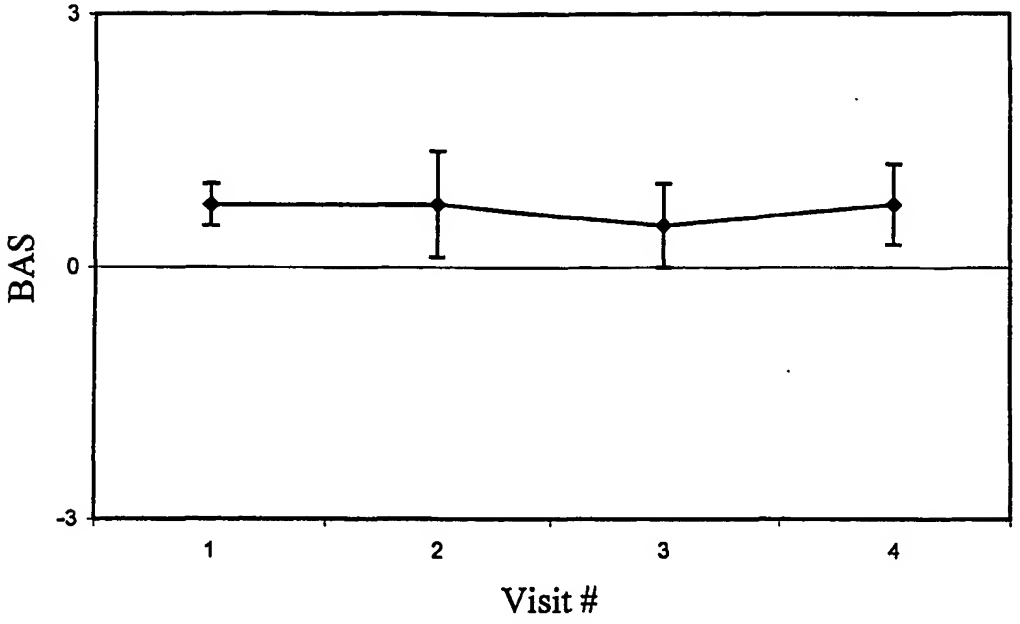


FIG. 11

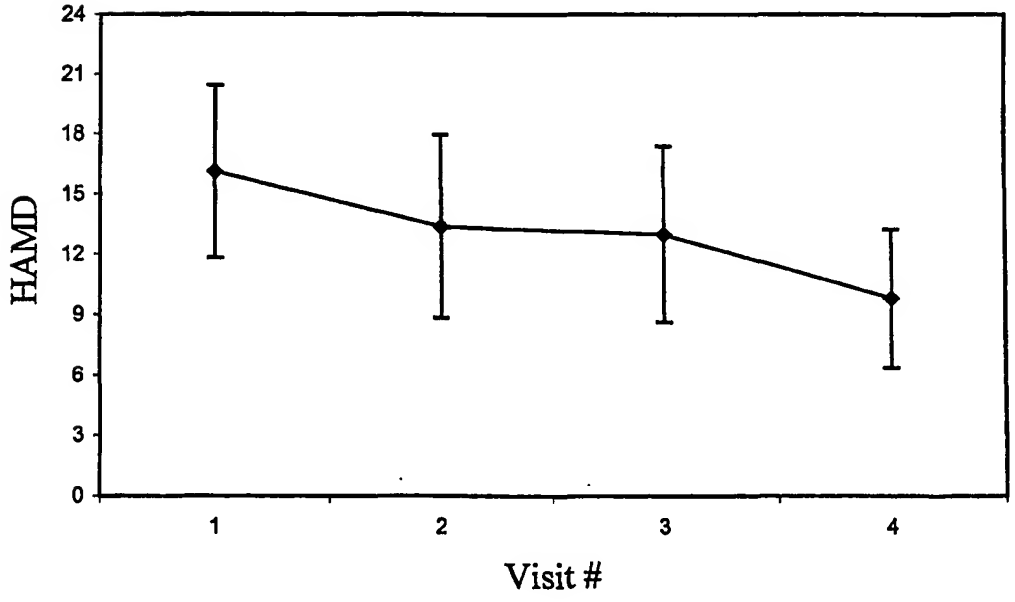


FIG. 12

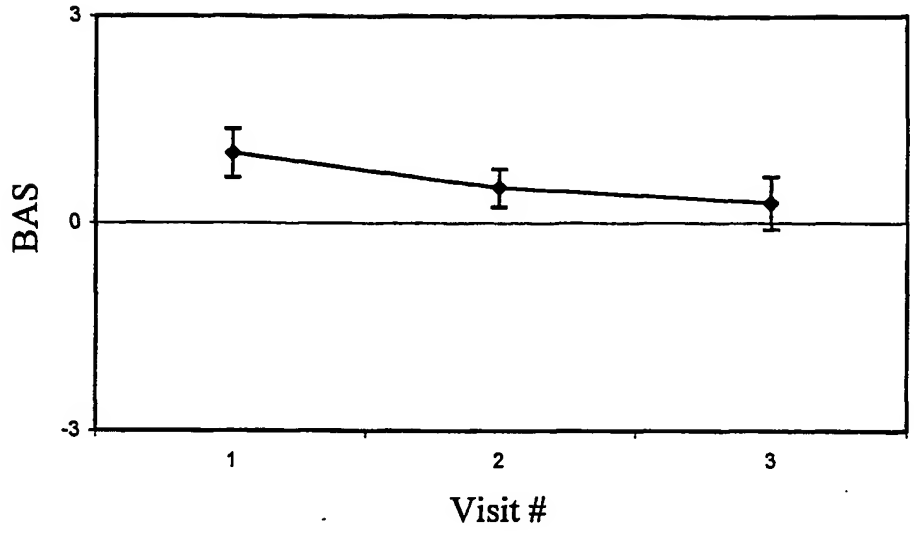


FIG. 13

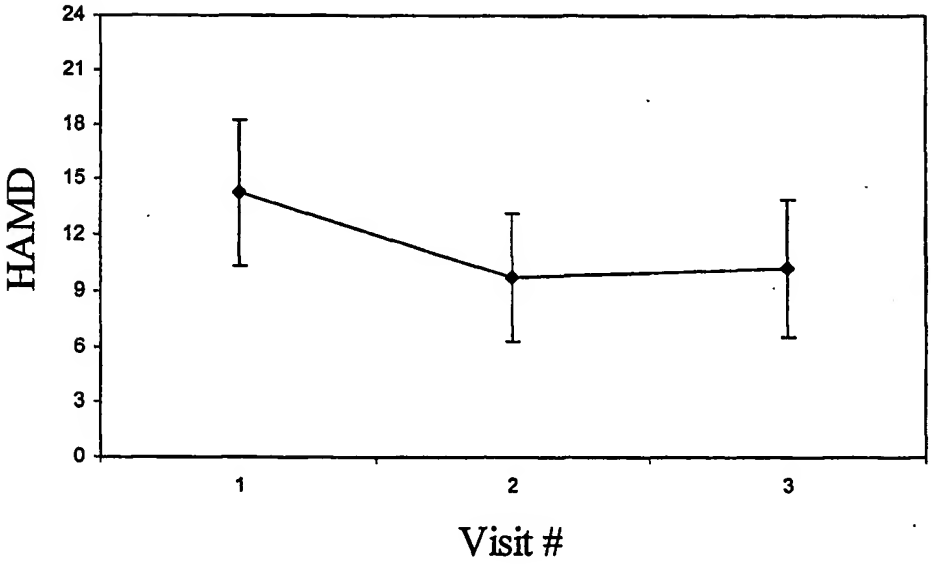


FIG. 14

FIG. 15

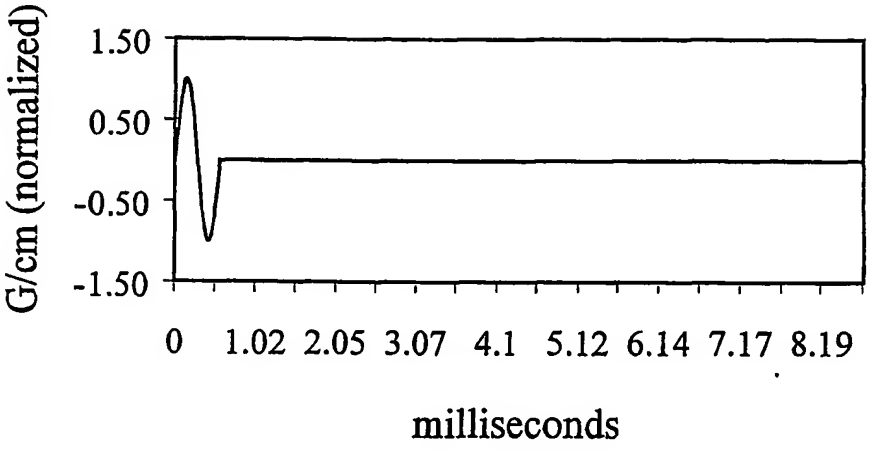

G/cm (normalized)
1.50
0.50
-0.50
-1.50
0
1.02
2.05
3.07
4.1
5.12
6.14
7.17
8.19
milliseconds

FIG. 16

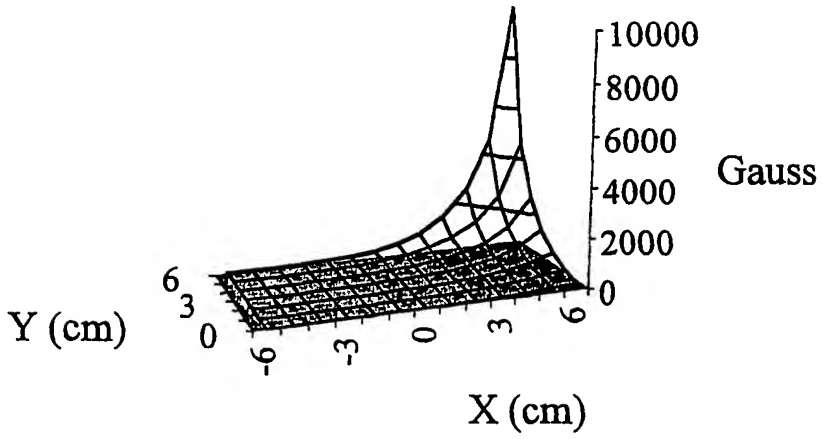

10000
8000
6000
4000
2000
0
Gauss
Y (cm)
6
3
0
-6
-3
0
3
6
X (cm)

FIG. 17

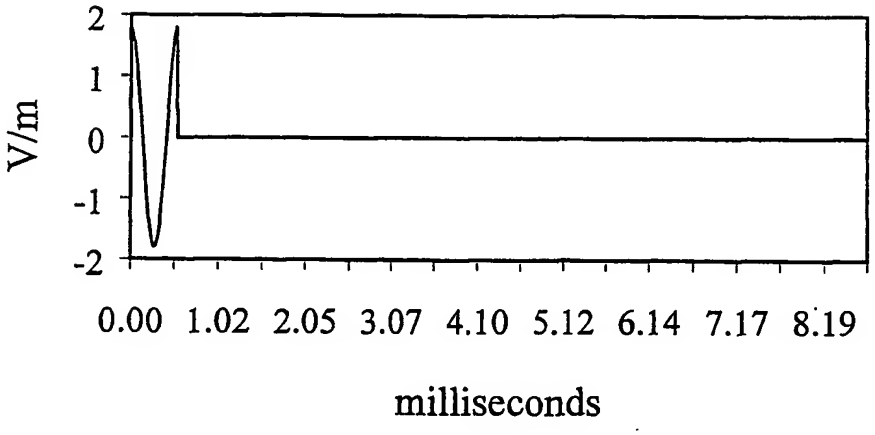


FIG. 18

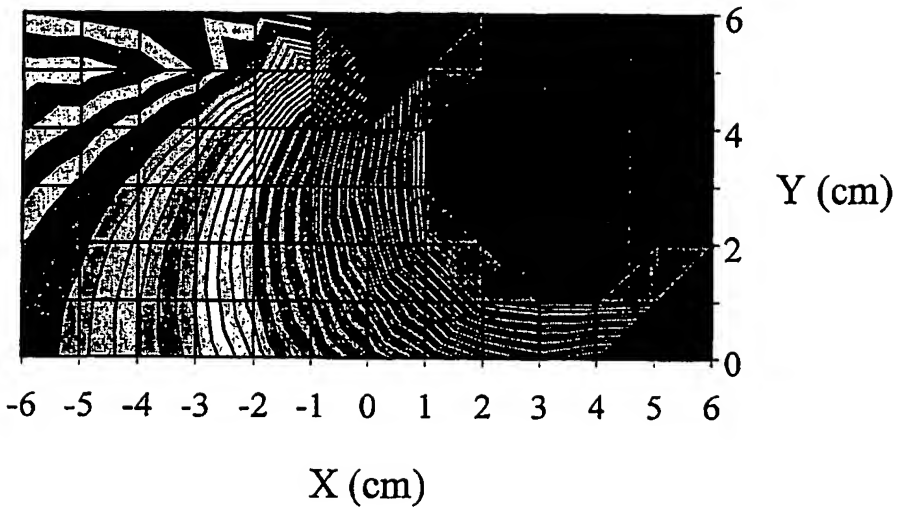


FIG. 19